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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,256	09/13/2005	Angus Moodycliffe	112843-066	3290

29157 7590 07/26/2007

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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
07/26/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PATENTS@BELLBOYD.COM

Office Action Summary	Application No.	Applicant(s)	
	10/525,256	MOODYCLIFFE ET AL.	
	Examiner	Art Unit	
	Dana Shin	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *4,5 and 9-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 6-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary, (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

This Office action is in response to the communications filed on June 18, 2007.

Currently, claims 1-32 are pending. Claims 4-5 and 9-32 have previously been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim.

The following rejections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to Arguments and Amendments

Applicant's arguments with respect to claims 1-3 and 6-8 have been considered but are moot in view of the new ground(s) of rejection. See below.

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 102

Claims 1-2, 6, and 8 remain rejected under 35 U.S.C. 102(a) as being anticipated by Deng et al. (*Glycobiology,* March 2002, 12:145-152), as evidenced by Nieda et al. (*Human Immunology,* 1999, 60:10-19) and Balreira et al. (*British Journal of Haematology,* 2005, 129:667-676) for the reasons of record as set forth in the Office action mailed on December 6, 2006 and for the reasons stated below.

Applicant's arguments filed on June 18, 2007 have been fully considered but they are not persuasive. Contrary to applicant's assertion that Deng et al. do not teach or suggest the use of a polynucleotide that is antisense to the glucosylceramide synthase mRNA for prevention or treatment of epithelial tissue damage, Deng et al. teach a composition comprising a glucosylceramide synthase antisense polynucleotide, which decreases the level of glucosylceramide expression and reduces melanoma formation (therefore, epithelial tissue damage) when administered *in vivo* in mice (pages 147-149). Accordingly, claims 1-2, 6, and 8 remain rejected.

New Rejections Necessitated by Amendments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3 and 7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 3 and 7 are currently amended to recite "wherein the polynucleotide is an RNAi oligonucleotide". However, the specification provides no disclosure of the claimed "RNAi oligonucleotide" and furthermore, applicant's arguments regarding claim amendments do not address the claimed subject matter, "RNAi oligonucleotide". Accordingly, it is concluded that neither the content of the specification nor applicant's arguments reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed RNAi oligonucleotide, and therefore, the newly amended claims introduce new matter.

Claims 1-3 and 6-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition for treating epithelial tissue damage caused by melanoma formation comprising an antisense polynucleotide against the glucosylceramide synthase mRNA, does not reasonably provide enablement for a composition for preventing any other epithelial tissue damage. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not

be undue experimentation. The key word is 'undue', not 'experimentation'." (Wands, 8 USPQ2d 1404). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The claims are currently amended to recite a composition for preventing or treating epithelial tissue damage wherein the composition is a polynucleotide antisense targeted to the glucosylceramide synthase mRNA, which prevents or treats epithelial tissue damage. As such, the claimed invention reads on a pharmaceutical composition for *in vivo* therapeutic application.

The specification provides neither the claimed composition comprising a polynucleotide antisense targeted to the glucosylceramide synthase mRNA nor a working example wherein the claimed composition prevents or treats epithelial tissue damage. The only compositions comprising "nucleotide sequences" are primer sequences for GAPDH and CD_{1d} used for RT-PCR, which bears no relevance to the claimed polynucleotide antisense composition that is targeted to the glucosylceramide synthase mRNA. As stated previously in the prior Office action, the specification merely states that the number of the glucosylceramide synthase transcripts may be reduced by designing a polypeptide antisense to at least a part of the glucosylceramide synthase gene or mRNA. See page 10. Further, this is the one and only occurrence where the term "glucosylceramide synthase" appears throughout the entire specification. In other words,

the specification lacks any guidance, direction, or working example, which shows how to make a antisense polynucleotide compound that "treats" and "prevents" epithelial tissue damage when administered *in vivo*.

Problems related to therapeutic use of nucleic acids were well known in the art at the time of invention. See for example Opalinska et al. (*Nature Reviews Drug Discovery*, 2002, 1:503-514). Such problems include the inability to specifically deliver an effective concentration of a nucleic acid to a target cell, such that a target gene is inhibited to a degree necessary to result in a therapeutic effect.

Opalinska et al. state on page 511

> "[I]t is widely appreciated that the ability of nucleic-acid molecules to modify gene expression *in vivo* is quite variable, and therefore wanting in terms of reliability. Several issues have been implicated as a root cause of this problem, including molecule delivery to targeted cells and specific compartments within cells and identification of sequence that is accessible to hybridization in the genomic DNA or RNA"

and in column 2 of the same page,

> "Another problem in this field is the limited ability to deliver nucleic acids into cells and have them reach their target. Without this ability, it is clear that even an appropriately targeted sequence is not likely to be efficient. As a general rule, oligonucleotides are taken up primarily through a combination of adsorptive and fluid-phase endocytosis. After internalization, confocal and electron microscopy studies have indicated that the bulk of the oligonucleotides enter the endosome-lysosome compartment, in which most of the material becomes either trapped or degraded."

In light of the fact that the specification is completely silent about the claimed composition for treating or preventing epithelial tissue damage, and the totality of the factors listed above, undue experimentation would have been necessary for one of ordinary skill in the art to make and use the claimed composition, and therefore it is concluded that the instantly claimed invention is enabled only insofar as what was known in the art at the time the invention was made. That is, the claimed composition is enabled only for a composition comprising a glucosylceramide synthase antisense polynucleotide for "treating" epithelial tissue damage

formed by melanoma. See the teachings of Deng et al. (see §102(a) rejection above).

Conclusion

No claim is allowed.

This application contains claims 4-5 and 9-32 drawn to inventions nonelected with traverse in the reply filed on November 13, 2006. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dana Shin whose telephone number is 571-272-8008. The examiner can normally be reached on Monday through Friday, from 8am-4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

/J. E. Angell/
Primary Examiner
Art Unit 1635